EXHIBIT 8

Europäisches Patentamt
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REÇU LE
15 SEP. 2008
ERNEST GUTMANN - YVES PLASSERAUD SAS

Date
16.09.08

Reference	Application No./Patent No.
B06617C-CA	07014859.8 - 2402 / 1900376
Applicant/Proprietor	
PROGENICS PHARMACEUTICALS, INC.	

Communication

The extended European search report is enclosed.

The extended European search report includes, pursuant to Rule 62 EPC, the European search report (R. 61 EPC) or the partial European search report/ declaration of no search (R. 63 EPC) and the European search opinion.

Copies of documents cited in the European search report are attached.

☑ 1 additional set(s) of copies of such documents is (are) enclosed as well.

The following have been approved:

☑ Abstract ☑ Title

☐ The Abstract was modified and the definitive text is attached to this communication.

The following figure(s) will be published together with the abstract:

Refund of the search fee

If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.

Europäisches Patentamt • European Patent Office • Office européen des brevets

Applicants: Graham P. Allaway et al.
Serial No.: 09/888,938
Filed: June 25, 2001
Exhibit 8

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 63 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 07 01 4859

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	WO 94/19017 A (PROGENICS PHARM INC [US]) 1 September 1994 (1994-09-01) * page 28, line 5 - page 39, line 16 * * table 2 * * figure 3 * * claims 1-27 * -----	1-15, 20-23, 36-64	INV. A61K39/21 A61K39/40 A61K39/42 C12N5/06 C12N7/00 C12N7/04 C12N7/06 C12Q1/70 A61K39/395 C07K16/28
X	TILLEY S A ET AL: "SYNERGISTIC NEUTRALIZATION OF HIV-1 BY HUMAN MONOCLONAL ANTIBODIES AGAINST THE V3 LOOP AND THE CD4-BINDING SITE OF GP120" AIDS RESEARCH AND HUMAN RETROVIRUSES, MARY ANN LIEBERT, US, vol. 8, no. 4, 1 April 1992 (1992-04-01), pages 461-466, XP002045539 ISSN: 0889-2229 * abstract * -----	1-15, 20-23, 36-64	
	-/--		

TECHNICAL FIELDS SEARCHED (IPC)

A61K
C07K

INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.

Claims searched completely :

Claims searched incompletely :

Claims not searched :

Reason for the limitation of the search:

see sheet C

Place of search	Date of completion of the search	Examiner
Munich	29 May 2008	Ulbrecht, Matthias

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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EPO FORM 1503 03.82 (P04E07)

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	BURKLY L ET AL: "SYNERGISTIC INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 ENVELOPE GLYCOPROTEIN-MEDIATED CELL FUSION AND INFECTION BY AN ANTIBODY TO CD4 DOMAIN 2 IN COMBINATION WITH ANTI-GP120 ANTIBODIES" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 69, no. 7, 1 July 1995 (1995-07-01), pages 4267-4273, XP000578381 ISSN: 0022-538X * abstract * * table 1 *	1-15, 20-23, 36-64	
X	WO 97/47318 A (PROGENICS PHARM INC ; AARON DIAMOND AIDS RESEARCH CE (US)) 18 December 1997 (1997-12-18) * tables 1,2 * * claims 42-48 *	1-15, 20-23, 36-64	TECHNICAL FIELDS SEARCHED (IPC)
A	WO 98/18826 A (LEUKOSITE INC) 7 May 1998 (1998-05-07) * page 9, line 1 - line 26 * * page 13, line 24 - page 18, line 10 * * page 45, line 4 - page 48, line 24 * * page 75, line 1 - page 76, line 5 * * claims 1-3,12,25,47,48 *	1-15, 20-23, 36-64	
A	WO 97/45543 A (COMBADIERE CHRISTOPHE ; FENG YU (US); US HEALTH (US); ALKHATIB GHALIB) 4 December 1997 (1997-12-04) * page 21, line 1 - page 25, line 16 * * page 28, line 25 - page 33, line 21 * * example 4 *	1-15, 20-23, 36-64	
	-/--		

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A,D	WU L ET AL: "CCR5 LEVELS AND EXPRESSION PATTERN CORRELATE WITH INFECTABILITY BY MACROPHAGE-TROPIC HIV-1, IN VITRO" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 185, no. 9, 5 May 1997 (1997-05-05), pages 1681-1691, XP002944844 ISSN: 0022-1007 * abstract * * page 1683, left-hand column, paragraph 4 - right-hand column, paragraph 1 * * page 1686, right-hand column, paragraph 2 - page 1687, left-hand column, paragraph 1 * * figure 6 *	1-15, 20-23, 36-64	
A	GHORPADE ANUJA ET AL: "Role of the beta-chemokine receptors CCR3 and CCR5 in human immunodeficiency virus type 1 infection of monocytes and microglia" JOURNAL OF VIROLOGY, vol. 72, no. 4, April 1998 (1998-04), pages 3351-3361, XP002296645 ISSN: 0022-538X * abstract * * page 3351, right-hand column, last paragraph * * page 3355, left-hand column, last paragraph - page 3357, left-hand column, paragraph 2 * * figures 6,7 *	1-15, 20-23, 36-64	TECHNICAL FIELDS SEARCHED (IPC)

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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	MCKNIGHT A ET AL: "INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS FUSION BY A MONOCLONAL ANTIBODY TO A CORECEPTOR (CXCR4) IS BOTH CELL TYPE AND VIRUS STRAIN DEPENDENT" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 71, no. 2, February 1997 (1997-02), pages 1692-1696, XP002921360 ISSN: 0022-538X * the whole document *	1-15, 20-23, 36-64	
A	YLISASTIGUI LOYDA ET AL: "Synthetic full-length and truncated RANTES inhibit HIV-1 infection of primary macrophages" AIDS (LONDON), vol. 12, no. 9, 18 June 1998 (1998-06-18), pages 977-984, XP009036542 ISSN: 0269-9370 * the whole document *	1-5,20, 22,23	TECHNICAL FIELDS SEARCHED (IPC)
A,D	SIMMONS G ET AL: "POTENT INHIBITION OF HIV-1 INFECTIVITY IN MACROPHAGES AND LYMPHOCYTES BY A NOVEL CCR5 ANTOGONIST" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 276, 1997, pages 276-279, XP000887293 ISSN: 0036-8075 * the whole document *	1-5,20, 22,23	

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EPO FORM 1503 03.82 (P04C10)

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A,D	DONZELLA G ET AL: "AMD3100, A SMALL MOLECULE INHIBITOR OF HIV-1 ENTRY VIA THE CXCR4 CO-RECEPTOR" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 4, no. 1, 1 January 1998 (1998-01-01), pages 72-77, XP002932484 ISSN: 1078-8956 * abstract *	1-4	
P,X	OLSON W C ET AL: "Differential inhibition of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal antibodies to CCR5" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 73, no. 5, May 1999 (1999-05), pages 4145-4155, XP002290005 ISSN: 0022-538X * the whole document *	1-15, 20-23, 36-64	TECHNICAL FIELDS SEARCHED (IPC)

EPO FORM 1503 03.82 (P04C10)

Although claims 63 and 64 are directed to a method of treatment of the human/animal body (Article 53(c) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

European Patent Office

Application Number
EP 07 01 4859

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☒ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

1-4, 63, 64 (all partially); 5-15, 20-23, 36-62 (all completely)

☐ The present supplementary European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims (Rule 164 (1) EPC).

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Invention 1: claims 1-4, 63, 64 (all partially); claims 5-15, 20-23, 36-62 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claims 5, 9, 46 and 58-62; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

Invention 2: claims 1-4, 63, 64 (all partially); claims 16-19 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 16; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

Invention 3: claims 1-4, 63, 64 (all partially); claims 24, 25 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 24; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

Invention 4: claims 1, 2, 63, 64 (all partially); claims 26-35 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 26; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Invention 5: claims 65-77 (all partially)

The anti-CCR5 monoclonal antibody PA8 and nucleic acids encoding it or fragments thereof.

Inventions 6-10: claims 65-77 (all partially)

Idem as invention 5, but each of inventions 6-10 referring to one of mAbs PA9-12 and PA14.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 07 01 4859

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

29-05-2008

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9419017 A	01-09-1994	AU 684073 B2	04-12-1997
		AU 6270894 A	14-09-1994
		CA 2156421 A1	01-09-1994
		EP 0687183 A1	20-12-1995
		US 5817767 A	06-10-1998
WO 9747318 A	18-12-1997	AU 3390297 A	07-01-1998
		AU 735460 B2	12-07-2001
		AU 3402697 A	07-01-1998
		CA 2257991 A1	18-12-1997
		EP 0956044 A1	17-11-1999
		JP 2001503608 T	21-03-2001
		WO 9747319 A1	18-12-1997
WO 9818826 A	07-05-1998	AU 5155398 A	22-05-1998
		US 2003166870 A1	04-09-2003
WO 9745543 A	04-12-1997	AU 3375697 A	05-01-1998
		EP 0975749 A2	02-02-2000

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

The examination is being carried out on the **following application documents**:

Description, Pages

1-47 as originally filed

Sequence listings part of the description, Pages

1, 2 as originally filed

Claims, Numbers

1-77 as originally filed

Drawings, Sheets

1/11-11/11 as originally filed

1. *Cited documents:*

D1: WO 94/19017 A (PROGENICS PHARM INC [US]) 1 September 1994 (1994-09-01)

D2: TILLEY S A ET AL: "SYNERGISTIC NEUTRALIZATION OF HIV-1 BY HUMAN MONOCLONAL ANTIBODIES AGAINST THE V3 LOOP AND THE CD4-BINDING SITE OF GP120" AIDS RESEARCH AND HUMAN RETROVIRUSES, MARY ANN LIEBERT, US, vol. 8, no. 4, 1 April 1992 (1992-04-01), pages 461-466, XP002045539 ISSN: 0889-2229

D3: WO 97/47318 A (PROGENICS PHARM INC ; AARON DIAMOND AIDS RESEARCH CE (US)) 18 December 1997 (1997-12-18)

D4: WO 98/18826 A (LEUKOSITE INC) 7 May 1998 (1998-05-07)

D5: WO 97/45543 A (COMBADIERE CHRISTOPHE ; FENG YU (US); US

HEALTH (US); ALKHATIB GHALIB) 4 December 1997 (1997-12-04)

D6: WU L ET AL: "CCR5 LEVELS AND EXPRESSION PATTERN CORRELATE WITH INFECTABILITY BY MACROPHAGE-TROPIC HIV-1, IN VITRO" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 185, no. 9, 5 May 1997 (1997-05-05), pages 1681-1691, XP002944844 ISSN: 0022-1007

D7: GHORPADE ANUJA ET AL: "Role of the beta-chemokine receptors CCR3 and CCR5 in human immunodeficiency virus type 1 infection of monocytes and microglia" JOURNAL OF VIROLOGY, vol. 72, no. 4, April 1998 (1998-04), pages 3351-3361, XP002296645 ISSN: 0022-538X

D8: MCKNIGHT A ET AL: "INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS FUSION BY A MONOCLONAL ANTIBODY TO A CORECEPTOR (CXCR4) IS BOTH CELL TYPE AND VIRUS STRAIN DEPENDENT" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 71, no. 2, February 1997 (1997-02), pages 1692-1696, XP002921360 ISSN: 0022-538X

D9: YLISASTIGUI LOYDA ET AL: "Synthetic full-length and truncated RANTES inhibit HIV-1 infection of primary macrophages" AIDS (LONDON), vol. 12, no. 9, 18 June 1998 (1998-06-18), pages 977-984, XP009036542 ISSN: 0269-9370

D10: SIMMONS G ET AL: "POTENT INHIBITION OF HIV-1 INFECTIVITY IN MACROPHAGES AND LYMPHOCYTES BY A NOVEL CCR5 ANTOGONIST" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 276, 1997, pages 276-279, XP000887293 ISSN: 0036-8075

D11: DONZELLA G ET AL: "AMD3100, A SMALL MOLECULE INHIBITOR OF HIV-1 ENTRY VIA THE CXCR4 CO-RECEPTOR" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 4, no. 1, 1 January 1998 (1998-01-01), pages 72-77, XP002932484 ISSN: 1078-8956

D12: BURKLY L ET AL: "SYNERGISTIC INHIBITION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 ENVELOPE GLYCOPROTEIN-MEDIATED CELL FUSION AND INFECTION BY AN ANTIBODY TO CD4 DOMAIN 2 IN COMBINATION WITH ANTI-GP120 ANTIBODIES" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 69, no. 7, 1 July 1995 (1995-07-01), pages 4267-4273, XP000578381 ISSN: 0022-538X

D13: OLSON W C ET AL: "Differential inhibition of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal antibodies to CCR5" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 73, no. 5, May 1999 (1999-05), pages 4145-4155, XP002290005 ISSN: 0022-538X

2. *Unity of invention (Art. 82 EPC):*

2.1 The Search Division considers the application to lack unity of invention and identifies the following inventions:

a) Invention 1: claims 1-4, 63, 64 (all partially); claims 5-15, 20-23, 36-62 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claims 5, 9, 46 and 58-62; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

b) Invention 2: claims 1-4, 63, 64 (all partially); claims 16-19 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 16; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

c) Invention 3: claims 1-4, 63, 64 (all partially); claims 24, 25 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds

prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 24; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

d) Invention 4: claims 1, 2, 63, 64 (all partially); claims 26-35 (all completely)

A composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or which inhibits fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as defined in claim 26; a method of treating a subject afflicted with HIV or of preventing a subject from contracting HIV-1 using said composition.

e) Invention 5: claims 65-77 (all partially)

The anti-CCR5 monoclonal antibody PA8 and nucleic acids encoding it or fragments thereof.

f) Inventions 6-10: claims 65-77 (all partially)

Idem as invention 5, but each of inventions 6-10 referring to one of mAbs PA9-12 and PA14.

2.2 The reasons for the objection as to lack of unity of invention are as follows:

a) The only identifiable technical feature that all inventions have in common is that they relate to compounds preventing the productive interaction between HIV-1 and an HIV-1 fusion co-receptor, wherein no particular limitation appears to be imposed by the term "co-receptor". Furthermore, inventions 1-4 all relate to compositions comprising at least two synergistically effective compounds. Moreover, inventions 5-10 all feature monoclonal antibodies (mAbs) specific for CCR5 which inhibit HIV-1 infection and/or fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell. Finally, the mAbs of inventions 5-9 do not antagonise RANTES.

b) These features cannot represent special technical features in the sense of R. 44(1)

EPC. D4 (Example 4; Fig. 8A, 10, 11); D5 (p. 21, l. 1 - p. 25, l. 16; Example 4); D6 (abstract; Fig. 6); and D7 (abstract; Fig. 5-7) teach CCR5-specific monoclonal antibodies which inhibit HIV-1 infection. Of these antibodies, at least mAb 2D7, taught by D2, has the inherent property of also inhibiting the fusion of HIV-1 or HIV-1 envelope glycoprotein-positive cells to target cells. Furthermore, D4, D6 and D7 disclose the mAb 3A9 which does not antagonise RANTES (cf. D4: Fig. 8A). D8 (abstract) discloses an anti-CXCR4 antibody that inhibits inter alia HIV-1 fusion. D2 (abstract) discloses a combination of human mAbs that target the V3 loop and the CD4-binding site of gp120 that synergistically neutralise HIV-1. D1 (Tab. 2) teaches a synergistic composition comprising an antibody targeting the V3 loop of HIV-1 gp120 and a CD4-based molecule that inhibits HIV-1 envelope-mediated cell fusion. D3 (Tab. 1 and 2) teaches a synergistic composition inhibiting HIV-1 envelope glycoprotein mediated membrane fusion as well as HIV-1 infection which comprises RANTES, MIP-1α and MIP-1β, all of which bind to CCR5. D9 (abstract) and D10 (abstract) teach the inhibition of HIV-1 infection by RANTES and its derivatives. D11 (abstract) teaches the inhibition of HIV-1 entry via the CXCR4 co-receptor by bicyclam AMD3100. D12 teaches a synergistic composition inhibiting HIV infection and envelope glycoprotein-mediated cell fusion which comprises an anti-gp120 and an anti-CD4 antibody (abstract).

c) In view of the prior art represented by D1-D12, the problem of the underlying application can be defined as the provision (i) of further compounds preventing the productive interaction between HIV-1 and an HIV-1 fusion co-receptor, thereby inhibiting HIV-1 infection or the fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell or (ii) of further synergistic combinations of such compounds.

d) Each of the inventions listed above represents an independent solution concerning one of the foregoing problems (i) or (ii) underlying the present application. Solution 1 is the provision of a composition comprising at least two synergistically active compounds for inhibiting HIV-1 infection or fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell, wherein at least one of said compounds prevents the productive interaction between HIV-1 and an HIV-1 fusion co-receptor as well as of the therapeutic use thereof, wherein at least one of the compounds is an antibody or comprises a portion thereof or a polypeptide which binds to a CCR5

epitope. Solution 2-4 are distinguished from solution 1 in that the at least one compound, respectively, is a chemokine or chemokine derivative; a nonpeptidyl molecule; and a compound that inhibits the attachment of HIV-1 to a target cell. Solutions 6-10 each provides one of the anti-CCR5 mAbs PA8-PA12 and PA14 as well as nucleic acids encoding at least parts thereof.

e) In view of the fact that compounds inhibiting the productive interaction between HIV-1 and an HIV-1 co-receptor, thereby inhibiting HIV-1 infection and/or fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell, including synergistic compositions of at least two such compounds, as well as monoclonal antibodies specific for CCR5 which inhibit HIV-1 infection and/or fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell, including such mAbs which do not antagonise RANTES, are already known from the prior art; and due to the fact that no other technical features can be distinguished which, in the light of the prior art could be regarded as special technical features common to the above solutions, the search division is of the opinion that there is no single inventive concept in the sense of Art. 82 EPC underlying the 10 solutions contained in the present application. Consequently, there is a lack of unity, and the different inventions have been formulated as different subjects on the communication pursuant R. 46 EPC.

f) The Search Division has searched invention 1 (claims 1-4, 63, 64 (all partially); claims 5-15, 20-23, 36-62 (all completely)).

2.3 Should the applicant not have a search report drawn up on the other inventions (R. 64 EPC), the application will have to be prosecuted on the basis of the invention in respect of which a search has already been carried out, in other words the invention first mentioned in the claims. The applicant should then limit the application to the invention searched and excise those parts of the application relating to the other inventions.

2.4 Should the applicant have any other invention searched he will have to indicate on which searched invention the further prosecution of the application should be based (cf. GL. C-III, 7.10). The applicant will be asked to state upon which invention further prosecution of this application should be based and to limit the application accordingly. Other inventions will have to be excised from the claims, description and

drawings if any.

2.5 The subject-matter to be excised may be made the subject of one or more divisional applications. The divisional applications must be filed with the European Patent Office in Munich, The Hague or Berlin and shall be in the language of the proceedings relating to the present application (cf. Art. 76(1) and R. 36(2) EPC). The time limit for filing divisional applications (R. 36(1) EPC) must be observed.

2.6 The following observations only relate to invention 1 (claims 1-4, 63, 64 (all partially); claims 5-15, 20-23, 36-62 (all completely))

3. *Priority (Art. 87 and 88 EPC):*

The claim to priority appears to be valid. Thus D13 does not constitute prior art under Art. 54(1) and (2) EPC.

4. *Exceptions to patentability (Art. 53(c) EPC):*

Claims 63 and 64 relate to subject-matter not susceptible to patentability. The claims have to be reformulated into a second medical use compliant with Art. 54(3) and (4) EPC.

5. *Clarity and support (Art. 84 EPC):*

5.1 Claims 1 and 2 define the compounds in terms of their properties without any structural limitation. The first compound is only required to synergistically inhibit HIV-1 infection or the fusion of HIV-1 or an HIV-1 envelope glycoprotein-positive cell to a target cell. The second compound is further defined as preventing the productive interaction between HIV-1 and an HIV-1 fusion co-receptor. By this claim language the claimed subject-matter is defined in terms of a result to be achieved. In particular as concerns the synergistic effects this definition amounts to a formulation of the underlying technical problem. Such a definition is not allowable pursuant GL. C-III, 4.10 as it is not determinable which compounds are actually covered by said claims. It would amount to an undue burden to test every conceivable compound for the said properties. This problem is not alleviated by the fact that claims 3 and 4 specify the

co-receptor. Also claims 36, 37 and 40 do not limit the claimed compounds by any structural features, but define further functional features which give way to structurally limitless embodiments thereof. Also for these claims it would amount to an undue burden to test every conceivable compound whether it fulfills the required properties. In conclusion, none of claims 1-4, 36, 37 and 40 allows to carry out a meaningful search covering the claims' entire scope. Consequently, the search of these claims was limited to embodiments which are clearly disclosed, namely those defined by the respective dependent claims suggesting structural limitations ie claims 5-10, 13, 28, 29 and 31-33, respectively.

5.2 The foregoing considerations equally apply to claims 63 and 64 as well as to claim 34 and its dependent claim 35 as claim 34 depends on claim 26 without proposing any structural features of the claimed compounds.

5.3 Claims 46-57 relate to a polypeptide that binds a CCR epitope. The binding properties of a polypeptide are ultimately defined by its amino acid sequence and are thus an inherent property of the said structural feature. Thus, without any pointer to the polypeptide's structural features no meaningful search covering the claims' whole scope could be performed. The search was thus limited to embodiments disclosed by the application, namely to antibodies having these binding properties.

5.4 Claims 11, 14, 23 and 44 relate to an "appropriate ratio". Either this ratio does not mean anything else than the "synergistically effective amount" suggested in claim 1, in which case these claims are redundant, or the claims lack clarity as it cannot be determined when a ratio has to be considered appropriate.

5.5 Claims 12, 15 and 45 which specify a ratio, suffer from the same deficiency as the claims they refer to. In addition, it is not determinable at which level (e.g. weight vs. molarity) the proposed values are to be achieved.

5.6 Claim 13 reads: "the antibody is ..." (emphasis added). The use of the singular is not consistent with its antecedent claim which proposes that "two or more compounds are antibodies" (emphasis added).

5.7 Claims 10 and 13 refer to antibodies indicated by generic names. These names do

not allow to determine which antibodies are actually covered. The requirement of clarity will only be met if the antibodies are designated by their respective deposit.

5.8 Claim 48 does not propose any limitation on claim 46 and thus appears to be redundant. It should be deleted for sake of conciseness.

6. *Sufficiency (Art. 83 EPC):*

The application discloses synergistic inhibition of HIV-1 fusion by the following combination of compounds:

PA12 and 2D7
PA12 and PA14
PA12 and RANTES
PA12 and CD4-IgG2

In contrast thereto, other combinations are either not synergistic (but e.g. additive) or even antagonistic, namely:

PA11 and PA12
PA14 and 2D7
PA14 and RANTES
2D7 and RANTES
PA14 and CD4-IgG2
2D7 and CD4-IgG2

It thus appears to be completely unpredictable and a matter of pure chance whether two compounds actually synergistically inhibit HIV-1 fusion. The application fails to provide any clear guidance how to obtain such synergistic combinations without undue burden for any other combination than those referred to above. As none of claims 1-15, 20-23 and 36-64 is limited to the embodiments actually shown to display these properties, but requires a testing therefore, the requirement of sufficiency is not met.

7. *Novelty (Art. 54(1) and (2) EPC):*

7.1 The term "HIV-1 fusion co-receptor" as defined at p. 10, l. 18-22 is not limited to

chemokine receptors, but appears to also cover CD4, as also derivable e.g. from embodiments falling under claims 1 and 2 suggested by claims 27, 29, 31 and 32. D1 discloses a synergistic composition inhibiting HIV-1 envelope-mediated cell fusion comprising a CD4-IgG2 molecule and a monoclonal antibody targeting either the V3 loop of HIV-1 gp120 or HIV-1 gp41 (p. 28, l. 5 - p. 39, l. 16; Tab. 2; Fig. 3; claims 1-27). The molar ratio of both compounds is appropriate to obtain said synergistic effect and ranges between 1:1.5 and 1:6 (cf. Tab. 2). This composition is used for the prevention and treatment of an HIV-1 infection. The V3 loop contains the binding site for CXCR4. Thus, the antibody used in D1 inherently abrogates the binding of gp120 to the HIV-1 fusion co-receptor CXCR4. On the other hand CD4-IgG2 also binds an HIV-1 fusion co-receptor (supra). Thus, the disclosure of D1 anticipates the subject-matter of claims 1-6, 36, 40-45 and 58-64.

7.2 D2 teaches a synergistic composition of two monoclonal antibodies, one targeting the V3 loop of gp120 and the other the CD4-binding site of gp120 (abstract). As synergy is obtained, the antibodies' ratio must be appropriate. For the reasons given under 7.1, the antibody targeting the V3 loop also abrogates binding to CRCX4. Hence, the disclosure of D2 takes away the novelty of claims 1-6, 9, 36, 40, 43, 44 and 58-62.

7.3 D3 teaches that the combination of RANTES, MIP-1α and MIP-1β synergistically inhibits the HIV-1 envelope glycoprotein mediated membrane fusion (Tab. 2). Also disclosed is the use of said combination of cytokines for the treatment or prophylaxis of HIV-1 infections (claims 47 and 48). Hence, D3 destroys the novelty of claims 1-4, 63 and 64.

7.4 D12 discloses a synergistic composition inhibiting HIV infection and envelope glycoprotein-mediated cell fusion which comprises an anti-gp120 mAb and an anti-CD4 mAb in a ratio of 1:1 (abstract; Tab. 1), thereby destroying the novelty of claims 1, 2, 5, 6, 9, 36, 37, 39 and 43-45.

7.5 The combinations of features suggested by any of claims 7, 8, 10-15, 20-23 and 46-57 are not disclosed in the prior art. These claims are thus novel.

8. *Inventive step (Art. 56 EPC):*

In view of D2, D3 and D12 which equally represent the closest prior art, the problem underlying any of claims 7, 8, 10-15, 20-23 and 46-57 may be formulated as the provision of alternative synergistic compositions inhibiting HIV-1 infection or the fusion of HIV-1 and/or an HIV-1 envelope glycoprotein-positive cell to a target cell. It follows from the considerations under 6. that this problem is not solved over the whole claims' scope. Thus, none of said claims merits an inventive step.

9. Should the applicant decide to file a request for examination in relation to the present application, the following should be noted:

9.1 The statements at p. 1, l. 6-9 are irrelevant and should be deleted (R. 48(1)(c) EPC).

9.2 The wording "incorporated herein by reference" or the like (p. 1, l. 15) should be deleted (cf. GL. C-II, 4.19).

9.3 The references to Figures and Tables as found in the description do not match the Figures as provided ie the numbering of Figures and Tables is not consistent.